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(4) **Melatonin derivatives for use in the therapy of sleep disorders and in pre-anaesthetic medication.**

(52) The present invention relates to new pharmaceutical compositions active in the therapy of sleep disorders comprising N-acetyl-5-methoxy-triptamine (melatonin) or one of its derivatives, preferably 2-iodo-N-acetyl-5-methoxy-triptamine (2-iodomelatonin), 2-bromo-N-acetyl-5-methoxy-triptamine (2-bromomelatonin), 2-chloro-N-acetyl-5-methoxy-triptamine (2-chloromelatonin) or 6-chloro-N-acetyl-5-methoxy-triptamine (6-chloromelatonin), at a dosage comprised between 10 and 100 mg, preferably comprised respectively between 20 and 80 mg between 10 and 20 mg and between 10 and 40 mg alone or in association with a benzodiazepinic derivative at a dosage comprised between 0.06 and 25 mg.

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## PARTIAL EUROPEAN SEARCH REPORT

which under Rule 45 of the European Patent Convention  
shall be considered, for the purposes of subsequent  
proceedings, as the European search report

Application Number

EP 92 10 7865

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int. Cl.5)
X	EP-A-0 126 630 (MONASH UNIVERSITY) * Whole document *	1,12	A 61 K 31/40
Y	WO-A-8 901 472 (NELSON RES. & DEVT. CO.) * Pages 1,2,4,5,8,9 *	1-22	
X	JOURNAL OF PINEAL RESEARCH, vol. 7, no. 2, 1989, pages 205-209, Alan R. Liss, Inc.; D. SUGDEN: "Antigonadal activity of the melatonin analogs 2-iodomelatonin and 2-chloromelatonin in the juvenile Djungarian hamster, Phodopus sungorus campbelli" * Whole document *	1,4,10	
			TECHNICAL FIELDS SEARCHED (Int. Cl.5)
			A 61 K
INCOMPLETE SEARCH			
<p>The Search Division considers that the present European patent application does not comply with the provisions of the European Patent Convention to such an extent that it is not possible to carry out a meaningful search into the state of the art on the basis of some of the claims</p> <p>Claims searched completely : Claims searched incompletely : 1-22 Claims not searched :</p> <p>Reason for the limitation of the search:</p> <p>In view of the large number of compounds which may be encompassed within the term "benzodiazepinic derivative" (claim 1), the search was limited to the compound mentioned in the description and examples (triazolam).</p>			
Place of search		Date of completion of the search	Examiner
THE HAGUE		17-08-1992	GAC G.
CATEGORY OF CITED DOCUMENTS		I : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document	
X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document			



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DOCUMENTS CONSIDERED TO BE RELEVANT			CLASSIFICATION OF THE APPLICATION (Int. Cl. 5)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
Y	SLEEP, vol. 13, no. 3, June 1990, pages 232-244, Raven Press, Ltd, New York, US; G. COPINSCHI et al.: "Effects of the short-acting benzodiazepine triazolam, taken at bedtime, on circadian and sleep-related hormonal profiles in normal men" * Whole document *	1-22	TECHNICAL FIELDS SEARCHED (Int. Cl. 5)
Y	LIFE SCIENCES, vol. 40, no. 15, 17th April 1987, pages 1537-1543, Pergamon Journals Ltd, US; B. SURANYI-CADOTTE et al.: "Coexistence of central and peripheral benzodiazepine binding sites in the human pineal gland" * Whole document *	1-22	
A	ENDOCRINOLOGIA JAPONICA, vol. 33, no. 3, June 1986, pages 405-414; M. KABUTO et al.: "Nocturnal enhancement of plasma melatonin could be suppressed by benzodiazepines in humans" * Whole document *	1-22	
X	BIOCHEMICAL PHARMACOLOGY, vol. 40, no. 12, 15th December 1990, pages 2701-2705, Pergamon Press plc, Oxford, GB; L.P. NILES et al.: "Pharmacological inhibition of forskolin-stimulated adenylate cyclase activity in rat brain by melatonin, its analogs, and diazepam" * Whole document *	1,4,6	